

A M E N D M E N T S

In the Claims:

1. (Currently amended) A process for the production of a biologically active protein, comprising:

expressing said protein as a heterologous protein in an expression system comprising a cultivated organism having one or more cells, wherein the protein is expressed as a substantially correctly folded protein precursor in inclusion bodies having an aqueous solubility in the cells of the organism;

regulating one or more cultivation parameters selected from the group consisting of temperature of cultivation, composition of cultivation medium, induction mode, principle of performing the fermentation, addition of an agent capable of causing stress, and co-expression of auxiliary proteins, wherein regulating the one or more parameters ~~affects the aqueous solubility of~~ increases the proportion of substantially correctly folded protein precursor present in the inclusion bodies in the cells, relative to the proportion of substantially correctly folded protein precursor present in inclusion bodies in cells of an organism not cultivated by regulating said parameters;

isolating the inclusion bodies from the cells of the organism;

optionally, washing the inclusion bodies;

solubilizing the substantially correctly folded protein precursor from the inclusion bodies under non-denaturing conditions; and

purifying the biologically active protein from the solubilized substantially correctly folded protein precursor, wherein the purified protein is biologically active.

2. (Canceled).

3. (Previously Presented) A process for the production of a protein according to claim 1, wherein the heterologous protein is selected from the group consisting of G-CSF, GM-CSF, M-CSF, EGF, HAS, DNase, FGF, TNF-alpha, TNF-beta, interferons, and interleukins.

4. (Previously Presented) A process for the production of a protein according to claim 1, wherein the selected heterologous protein is G-CSF.

5. (Previously Presented) A process for the production of a protein according to claim 1, wherein the cultivated organism is selected from the group consisting of bacteria and yeasts.

6. (Previously Presented) A process for the production of a protein according to claim 5, wherein the cultivated organism is the bacterium *E. coli*.

7. (Previously Presented) A process for the production of a protein according to claim 1, wherein the heterologous protein is accumulated in the inclusion bodies to a proportion of at least about 10%, relative to the total protein mass of a cell of the organism used in the expression system.

8. (Canceled).

9. (Canceled).

10. (Currently Amended) A process according to claim 1, wherein the temperature of cultivation ranges from about 20° C. to about 30° C.

11. (Canceled).

12. (Previously Presented) A process according to claim 1, wherein regulating the induction mode comprises selecting an inducer from the group consisting of IPTG, lactose, and NaCl.

13. (Previously Presented) A process according to claim 12, wherein the selected inducer is IPTG.

14. (Previously Presented) A process according to claim 13, wherein the concentration of IPTG ranges from about 0.1 mM to about 1 mM.

15. (Previously Presented) A process according to claim 14, wherein the concentration of IPTG is about 0.4 mM.

16. (Previously Presented) A process according to claim 12, wherein the regulation of the induction mode further comprises adding the inducer at the beginning of the fermentation.
17. (Previously Presented) A process according to claim 1, wherein the principle of performing the fermentation is selected from the group consisting of performing of fermentation in a batch mode, performing of fermentation in a fed batch mode and performing of fermentation in one or more shake flasks.
18. (Canceled).
19. (Previously Presented) A process according to claim 1, wherein the composition of the cultivation medium is selected from the group consisting of GYST, GYSP, LYSP, LYST, LBON and GYSPON.
20. (Previously Presented) A process according to claim 19, wherein the selected medium is GYST, or GYSP.
21. (Previously Presented) A process according to claim 1, wherein the agent additive which is capable of causing stress is selected from the group consisting of ethanol and propanol.
22. (Canceled).
23. (Previously Presented) A process according to claim 1, wherein the step of washing comprises contacting the inclusion bodies with a solution selected from the group consisting of Tris/HCl buffer, phosphate buffer, acetate buffer, citrate buffer and water.
24. (Previously Presented) A process according to claim 23, wherein the concentration of the selected buffer ranges from about 1 mM to about 10 mM.

25. (Previously Presented) A process according to claim 23, wherein the selected solution is water.
26. (Currently Amended) A process for production of a protein according to claim 1, wherein the step of solubilizing the substantially correctly folded protein precursor from the inclusion bodies further comprises contacting the inclusion bodies with a non-denaturing solution selected from the group consisting of: urea ranging in concentration from about 1M to about 2M, N-lauroyl sarcosine ranging in concentration from about 0.05% to about 0.25% mass per volume, betain, sarcosine, carbamoyl sarcosine, taurine, DMSO, non-detergent sulfobetains, and a buffer in a high, solubilising concentration, said buffer being selected from the group consisting of HEPES, HEPPS, MES, and ACES.
- 27-37. (Canceled).
38. (New) The process of claim 26, wherein the non-denaturing solution is N-lauroyl sarcosine.
39. (New) The process of claim 38, wherein the concentration of N-lauroyl sarcosine further ranges from about 0.1% to about 0.25% mass per volume.